Scientific Organizers:
Andrew May, Chan Zuckerberg Biohub, USA
Rodolphe Barrangou, North Carolina State University, USA
Knut Woltjen, CiRA, Kyoto University, Japan

The use of programmable nucleases such as CRISPR-Cas systems, ZFNs and TALENs has revolutionized cell biology by providing the ability to manipulate specific genetic and epigenetic states within living cells. These systems have been broadly applied as tools in research settings and increasingly are being used to develop improved models of disease and engineer cells for therapeutic purposes. Together with other DNA-modifying systems such as recombinases, integrases and transposases, it is now possible to introduce mutations that will model human disease, build complex synthetic signaling networks to perform regulated functions, and design cells to target specific disease states. Improvements to the methods involved requires understanding enzyme structures and mechanisms and how they intersect with cellular DNA repair systems. The intersection of this basic science with engineering approaches and improved cellular models is revolutionizing our understanding and treatment of human disease. The goal of this Keystone Symposia conference is to bring together those developing and studying genome engineering tools with groups who are applying them to build new disease models, identify disease mechanisms and drug targets, and develop cell-based therapeutics and genetic medicines. In addition to covering engineering of human and animal cells, this conference will also highlight the emerging field of genome engineering to identify new anti-microbial and anti-viral drugs and applications toward next-generation antibiotics. Invited talks will explore a broad range of topics covering new technologies, fundamental basic research, through the development of screening approaches, stem cell-based models of disease and design, and development of cellular therapeutics.

Plenary Session Topics:
- Genome Engineering Tools and Technologies
- Workshop 1: Tools and Technologies
- Structure and Mechanism of Genome Editing Systems
- Engineered Models of Genetic Disease
- Workshop 2: Delivery
- Design and Engineering of Cellular Devices
- Genome Editing Screens for Function and Disease Mechanisms
- Harnessing DNA Repair Mechanisms for Genome Engineering
- Genome Engineering of Bacteria for Therapeutic and Diagnostic Applications
- Workshop 3: Clinical Trial Update
- Genome Editing for Treating Human Disease

Discounted Registration Deadline: Dec 19, 2018
Visit [www.keystonesymposia.org/19B4](http://www.keystonesymposia.org/19B4) for more details.
TUESDAY, FEBRUARY 19
Arrival and Registration

WEDNESDAY, FEBRUARY 20
Welcome and Keynote Address
*Andrew May, Sana Biotechnology, Inc., USA
Philip D. Gregory, Bluebird Bio, Inc. Toward Therapeutic Genome Editing: A Brief History (And Some Lessons Learned from Classical Gene Therapy)

Genome Engineering Tools and Technologies
*Dana Carroll, University of Utah School of Medicine, USA
Prashant Mali, University of California, San Diego, USA Therapeutic Strategies via Genome Engineering: New Approaches and New Challenges
Charles Gersbach, Duke University, USA Epigenome Editing for Gene Therapy, Cell Programming and Functional Epigenomics
Alexis C. Komor, University of California, San Diego Using Uracil as a Genome Editing Intermediate
Peter Cameron, Caribou Biosciences, Inc., USA Short Talk: Harnessing Type I CRISPR–Cas Systems for Human Genome Engineering

Workshop 1: Tools and Technologies
*Joanne Kamens, Addgene, USA
Abigail R. Lambert, Fred Hutchinson Cancer Research Center, USA Structural and Functional Properties of Wild-Type and Engineered Meganucleases and MegaTALs
Henriette O’Green, University of California, Davis, USA Engineering Epigenetic Memory Requires Co-Targeting of Histone Methyltransferases and DNA Methyltransferases
Alister Funnell, Altius Institute for Biomedical Sciences, USA Rapid Single-Cell Quantification of On- and Off-Target Nuclease Activity
Janin Grajcarek, Kyoto University, Japan Identification of Microhomology-Flanked Deletion Mutations Across the Human Genome Enables Efficient Creation of Isogenic Disease Models in hiPSCs by CRISPR/Cas9
Hien Bao Dieu Thai, Korea Institute of Science and Technology, South Korea DNAzymes-Based Tetrahedral Nanostructure for Enhanced Intracellular Gene-Silencing Activity
Brock Roberts, Allen Institute for Cell Science, USA Systematic Gene Tagging to Illuminate Stem Cell Organization

Structure and Mechanism of Genome Editing Systems
*Maria Jasin, Memorial Sloan Kettering Cancer Center, USA
Benjamin P. Kleinstiver, Massachusetts General Hospital, USA Engineered CRISPR Nucleases to Enhance Genome Editing
Osamu Nureki, University of Tokyo, Japan Molecular Mechanism of CRISPR and Structure-Based Development of Genome Editing Tool toward Medical Applications

Edward J. Rebar, Sangamo Therapeutics, Inc., USA Short Talk: Optimizing Nuclease Specificity for Gene Editing via Tuning of Cleavage Kinetics Enables Complete Gene Modification with No Detectable Off-Targets
Amit Choudhary, Harvard Medical School, USA Short Talk: Synthetic Activators, Inhibitors and Degraders of CRISPR-Associated Nucleases

THURSDAY, FEBRUARY 21
Engineered Models of Genetic Disease
*Bruce R. Conklin, University of California, San Francisco, USA
Danwei Huangfu, Memorial Sloan Kettering Cancer Institute, USA Human Pluripotent Stem Cells as a Genetic Model for Human Development and Disease
Knut Woltjen, CiRA, Kyoto University, Japan Precise Human Disease Allele Creation and Correction through Microhomology-Mediated End Joining
Amy J. Wagers, Harvard University, USA Gene Editing in Stem Cells
Erika Sasaki, Central Institute for Experimental Animals, Japan Development of Genetically Modified Non-Human Primate Disease Models
Diogo Mosqueira, University of Nottingham, UK Short Talk: CRISPR/Cas9 Genome Editing in Human Pluripotent Stem Cells-Cardiomyocytes to Model and Treat Hypertrophic Cardiomyopathy

Poster Session 2
Design and Engineering of Cellular Devices
*Alexis C. Komor, University of California, San Diego, USA
Wilson Wong, Boston University, USA Mammalian Cell Design Using Synthetic Biology
Timothy K. Lu, Massachusetts Institute of Technology, USA Synthetic Gene Circuits for Next-Generation Therapeutics
Zoltan Ivics, Paul Ehrlich Institute, Germany Transposons: Molecular Parasites Tamed for Advanced Genome Engineering
Yale S. Michaels, University of Oxford, UK Short Talk: A Generalizable Method for Precisely Tuning Gene Expression Levels in Mammalian Cells with Engineered MicroRNA Target Sites

FRIDAY, FEBRUARY 22
Genome Editing Screens for Function and Disease Mechanisms
*Danwei Huangfu, Memorial Sloan Kettering Cancer Institute, USA
Fyodor D. Urnov, University of California, Berkeley, USA Editing Human Genome Control Circuits to Reveal Disease Mechanisms and Targets for Intervention in the Clinic
Jan E. Carente, Stanford University, USA CRISPR-Cas Screens for Studying Virus-Host Interactions

*Session Chair † Invited but not yet accepted  Program current as of September 13, 2019 Program subject to change. Meal formats are based on meeting venue.
For the most up-to-date details, visit www.keystonesymposia.org/19B4.
Nozomu Yachie, University of Tokyo, Japan
Tracing Dynamics of Cells and Molecules using DNA Barcodes and Genome Editing

Britt S. Adamson, Princeton University, USA
Mapping the Processes of Genome Editing with High-Resolution Functional Genomics

Take the Bull by the Horns: Steps to a Fulfilling Career in Science
* Joanne Kamens, Addgene, USA

Harnessing DNA Repair Mechanisms for Genome Engineering
*Brett S. Adamson, Princeton University, USA
Maria Jasinski, Memorial Sloan Kettering Cancer Center, USA
Homologous Recombination and End-Joining Mechanisms in Genome Editing

Beekie Wierter, University of California, Berkeley, USA
Unbiased Detection of CRISPR Off-Targets in vivo using DISCOVER-Seq

Nancy Maizels, University of Washington School of Medicine, USA
Gene Correction at Targeted DNA Breaks

Andrew May, Sana Biotechnology, Inc., USA
DNA Repair Outcomes Provide Insight into Genome Editing Mechanisms in Primary Cell Systems

Tetsuji Sakuma, Hiroshima University, Japan
Short Talk: Concurrent MMEJ-Assisted Fusional Knock-In of Long Gene Cassette in Human Cells

SATURDAY, FEBRUARY 23

Genome Engineering of Bacteria for Therapeutic and Diagnostic Applications
*Andrew May, Sana Biotechnology, Inc., USA
Rodolphe Barrangou, North Carolina State University, USA
Engineering Lactobacilli for Human Health Applications
Jason M. Peters, University of Wisconsin-Madison, USA
Bacterial CRISPR Screens to Identify the Mode of Action of Novel Antibiotics
Richard P. Novick, New York University, USA
Conversion of Staphylococcal Pathogenicity Islands to CRISPR-Cas9-Based Antibacterial Drones
Joel Berry, Caribou Biosciences, USA
Short Talk: Utilizing CRISPR-Based Genome Editing for Microbiome Engineering

Akos Nyerges, Hungarian Academy of Sciences, Hungary
Short Talk: Predicting Antibiotic Resistance by Targeted Mutagenesis and Directed Evolution in Pathogenic Bacteria
David R. Edgell, University of Western Ontario, Canada
Short Talk: High Efficiency Inter-Species Conjugal Transfer of a CRISPR Nuclease for Targeted Bacterial Elimination

Workshop 2: Delivery Methods
*Shondra M. Pruett-Miller, St. Jude Children’s Research Hospital, USA

Dana V. Foss, University of California, Berkeley, USA
Engineering Cas9 for T-Cell Specific Uptake and Therapeutic Genome Editing

Jacquelyn L S Hanson, SQZ Biotechnologies, USA
Microfluidic Delivery of Bioactive Molecules via SQZ Platform Enables Efficient T Cell Genome Engineering with Preserved Functionality

Lauren Elizabeth Woodard, Vanderbilt University, USA
Less Is More: How Less Recombinease Expression Produces More Genome-Modified Cells

Taisuke Kato, Niigata University, Japan
Gene Therapy for DRPLA Model Mice by AAV-Delivered CRISPR / Cas9

Eric Aird, University of Minnesota, USA
Enhancing HDR Efficiency by Tethering DNA to Cas9 via a Fused HUH Endonuclease

Erin Morgan, University of California, Santa Barbara, USA
Controlling the Genome: Light-Activated Delivery of Gene Editing Proteins and siRNA Allows for Up and Down Regulation of the Genome using Hollow Gold Nanoparticles

Masato Ohtsuka, Tokai University, Japan
i-GONAD: A Method for Generation of Genome-Edited Rodents without ex vivo Handling of Embryos

Anthony L. Forget, Intellia Therapeutics, USA
Supra-Therapeutic Levels of Transgene Expression Achieved in vivo by CRISPR/Cas9 Mediated Targeted Gene Insertion

Genome Editing for Treating Human Disease
*Fyodor D. Urnov, University of California, Berkeley, USA
Bruce R. Conklin, University of California, San Francisco, USA
Using Patient-Derived iPSC Tissues to Model Precise Genome Surgery

Leonela Amoasii, Exonics Therapeutics, USA
Gene Editing Restores Dystrophin Expression in a Canine Model of Duchenne Muscular Dystrophy

Lukas Jeker, University of Basel, Switzerland
Short Talk: Repairing Foxp3 Mutations in T Cells Restores Regulatory T Cell Function

Jorge Mansilla-Soto, Memorial Sloan Kettering Cancer Center, USA
Advancing CAR-T Therapy with Precise Genome Engineering

Vic E. Myer, Editas Medicine, USA
Controlling Rearrangement Frequencies in the Context of Multigene Genome Editing

Meeting Wrap-Up: Outcomes and Future Directions (Organizers)

SUNDAY, FEBRUARY 24

Departure